

1600RE 1

08/485943

GATATCCCTGCTCCAGCAGCTGCAAGGCTGCAAGAAAGAAAGATCCCAAGGAGCAAAATCTG 120  
 M C 1  
 CTGAGAGCCCTGTGTCTGGTTCTGTGCTGTTGGTCTTATCTGTCTTATGTTCAAGCACT 180  
 M R D L C R P L M L M E Y L E V V Q A V 22  
 GCCTATCCAGAAAGCTCAGGATGACACCAAAACCCCTCATCAAGACCATGTCACCAAGATP 240  
 P I Q K V Q D D F K T L I K T I V F R I 42  
 CAATGACATTTACACACAGCAGTCCGATATCCGCCAAGCAGAGGCTCACTGGCTTGGACTT 300  
 N D I S H T Q S V S A K Q R V T G L D V 62  
 CATTTCTTUGCTTACCUUATTTCTCTTTTGTCCAAATGACACCACTCTGCTGCTCTA 360  
 I F Q L M P I L S L S K M D Q T L A V Y 82  
 TCAACAGGCTCTCACCAGCTGCTTCCCAAAATGCTGCTGAGATAGCCAAATGACCTGGA 420  
 Q Q V L T S L P S Q N V L Q I A N D L E 102  
 GAATCTCCGAGACCTCTCTCCATCTCTGCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT 480  
 N L L D L L H L L A P S K S C S L P Q T 122  
 CAGTGGCTCTCAGAAAGCCAGAGAGCTGATGATGATGATGATGATGATGATGATGATGATGAT 540  
 S Q L Q K P E S L D Q V L E A E L Y S T 142  
 AAGAGTGGTGGCTTCTGAGCAGCTCTGAGCCTCTCTGCTCAGCAGCATTTCTCAACAGTTGGA 600  
 E V V A L S R L Q C S L Q D I L Q Q L D 162  
 TCTTACCCCTCAATGCTCAAGTTTCAAAAGCCACCCAGGCTCCCAAGAAATCATGTAAAGGG 660  
 V S P E C 167  
 AAGAAACCTTGGCTTCCAGCCTCTCTTCAAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC 720  
 TCATTTCTCTCCCTCTCTGATACCCACCCATCCAAAGGCATGAGTCCACAAATGCTTUAATC 780  
 AAGTTATGACACAACTTCATGAGCACAAAGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGG 840  
 CTAGTTCTTACGAAGTAGAGATAGACCCCATCCCATCCCTCTCATGTCGACCTGCTGCTGCT 900  
 GGGTACATGTTCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 960  
 TGGTAGAGCTTTTGGCTCTCTCAGAGCTTTTGGAGCAGCAGCAGCAGCAGCAGCAGCAGCAG 1020  
 CACAGTTCGAAACTCCCAAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC 1080  
 TATTTTGCATGATCTGAAGCAGGCACTCACTTTTTCAGCCTTTGCGCTCAGCAGCAGCAGC 1140  
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 GAAGGATCCGGAAGTCTCTCTCAATTACATATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1500  
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 ACTTGCAGCTGATTTTCCAGCATCTGAGGCT 2882

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## Figure 2

---G--GTTG CAAGGCCCAA GAAGCCCA-- -TCCTGGGAA GGAAAATGCA	50
TTGGGGAACC CTGTG-CGGA TTCTTGTGGC TTTGGCCCTA TCTTTTCTAT	100
GTCCAAGCTG TGCCCATCCA AAAAGTCCAA GATGACACCA AAACCCTCAT	150
CAAGACAATT GTCACCAGGA TCAATGACAT TTCACACACG CAGTCAGTCT	200
CCTCCAAACA GAAAGTCACC GGTTTGGACT TCATTCCCTGG GCTCCACCCC	250
ATCCTGACCT TATCCAAGAT GGACCAGACA CTGGCAGTCT ACCAACAGAT	300
CCTCACCAGT ATGCCTTCCA GAAACGTGAT CCAAATATCC AACGACCTGG	350
AGAACCTCCG GGATCTTCTT CACGTGCTGG CCTTCTCTAA GAGCTGCCAC	400
TTGCCCTGGG CCAGTGGCCT GGAGACCTTG GACAGCCTGG GGGGTGTCCT	450
GGAAGCTTCA GGCTACTCCA CAGAGGTGGT GGCCCTGAGC AGGCTGCAGG	500
GGTCTCTGCA GGACATGCTG TGGCAGCTGG ACCTCAGCCC TGGGTGCTGA	550
GGCCTTGAAG GTCACTCTTC CTGCAAGGAC T-ACGTTAAG GGAAGGAACT	600
CTGGTTTCCA GGTATCTCCA GGATTGAAGA GCATTGCATG GACACCCCTT	650
ATCCAGGACT CTGTCAATTT CCCTGACTCC TCTAAGCCAC TCTTCCAAAG	700
G	701

## Figure 3

1 Met His Trp Gly Thr Leu Cys Gly Phe Leu Trp Leu Trp Pro Tyr  
16 Leu Phe Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp  
31 Thr Lys Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile  
46 Ser His Thr Gln Ser Val Ser Ser Lys Gln Lys Val Thr Gly Leu  
61 Asp Phe Ile Pro Gly Leu His Pro Ile Leu Thr Leu Ser Lys Met  
76 Asp Gln Thr Leu Ala Val Tyr Gln Gln Ile Leu Thr Ser Met Pro  
91 Ser Arg Asn Val Ile Gln Ile Ser Asn Asp Leu Glu Asn Leu Arg  
106 Asp Leu Leu His Val Leu Ala Phe Ser Lys Ser Cys His Leu Pro  
121 Trp Ala Ser Gly Leu Glu Thr Leu Asp Ser Leu Gly Gly Val Leu  
136 Glu Ala Ser Gly Tyr Ser Thr Glu Val Val Ala Leu Ser Arg Leu  
151 Gln Gly Ser Leu Gln Asp Met Leu Trp Gln Leu Asp Leu Ser Pro  
166 Gly Cys End

## Figure 4

Mouse	MCWRPLCRFL WLWSYLSYVQ AVPIQKVQDD TKTLIKTI VT RINDISHTQS	50
	* * * * *	
Human	MHWGTL CGFL WLWPYLFYVQ AVPIQKVQDD TKTLIKTI VT RINDISHTQS	
Mouse	VSAKQRVTGL DFIPGLHPIL SLSKMDQTLA VYQQVLTSLP SQNVLQIAND	100
	* * * * *	
Human	VSSKQKVTGL DFIPGLHPIL TLSKMDQTLA VYQQILTSMPSRNVIQISND	
Mouse	LENLRDLLHL LAFSKSCSLP QTSGLQKPES LDGVLEASLY STEVVALSRL	150
	- * * * * - * *	
Human	LENLRDLLHV LAFSKSCHLP WASGLETLDS LGGVLEASGY STEVVALSRL	
Mouse	QGS LQDILQQ LDVSPEC	167
	- * - *	
Human	QGS LQDMLWQ LDLSPGC	

## Figure 5

1 Met Cys Trp Arg Pro Leu Cys Arg Phe Leu Trp Leu Trp Ser Tyr  
16 Leu Ser Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp  
31 Thr Lys Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile  
46 Ser His Thr Ser Val Ser Ala Lys Gln Arg Val Thr Gly Leu Asp  
61 Phe Ile Pro Gly Leu His Pro Ile Leu Ser Leu Ser Lys Met Asp  
76 Gln Thr Leu Ala Val Tyr Gln Gln Val Leu Thr Ser Leu Pro Ser  
91 Gln Asn Val Leu Gln Ile Ala Asn Asp Leu Glu Asn Leu Arg Asp  
106 Leu Leu His Leu Leu Ala Phe Ser Lys Ser Cys Ser Leu Pro Gln  
121 Thr Ser Gly Leu Gln Lys Pro Glu Ser Leu Asp Gly Val Leu Glu  
136 Ala Ser Leu Tyr Ser Thr Glu Val Val Ala Leu Ser Arg Leu Gln  
151 Gly Ser Leu Gln Asp Ile Leu Gln Gln Leu Asp Val Ser Pro Glu  
166 Cys End

## Figure 6

1 Met His Trp Gly Thr Leu Cys Gly Phe Leu Trp Leu Trp Pro Tyr  
16 Leu Phe Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp  
31 Thr Lys Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile  
46 Ser His Thr Ser Val Ser Ser Lys Gln Lys Val Thr Gly Leu Asp  
61 Phe Ile Pro Gly Leu His Pro Ile Leu Thr Leu Ser Lys Met Asp  
76 Gln Thr Leu Ala Val Tyr Gln Gln Ile Leu Thr Ser Met Pro Ser  
91 Arg Asn Val Ile Gln Ile Ser Asn Asp Leu Glu Asn Leu Arg Asp  
106 Leu Leu His Val Leu Ala Phe Ser Lys Ser Cys His Leu Pro Trp  
121 Ala Ser Gly Leu Glu Thr Leu Asp Ser Leu Gly Gly Val Leu Glu  
136 Ala Ser Gly Tyr Ser Thr Glu Val Val Ala Leu Ser Arg Leu Gln  
151 Gly Ser Leu Gln Asp Met Leu Trp Gln Leu Asp Leu Ser Pro Gly  
166 Cys End

Figure 7

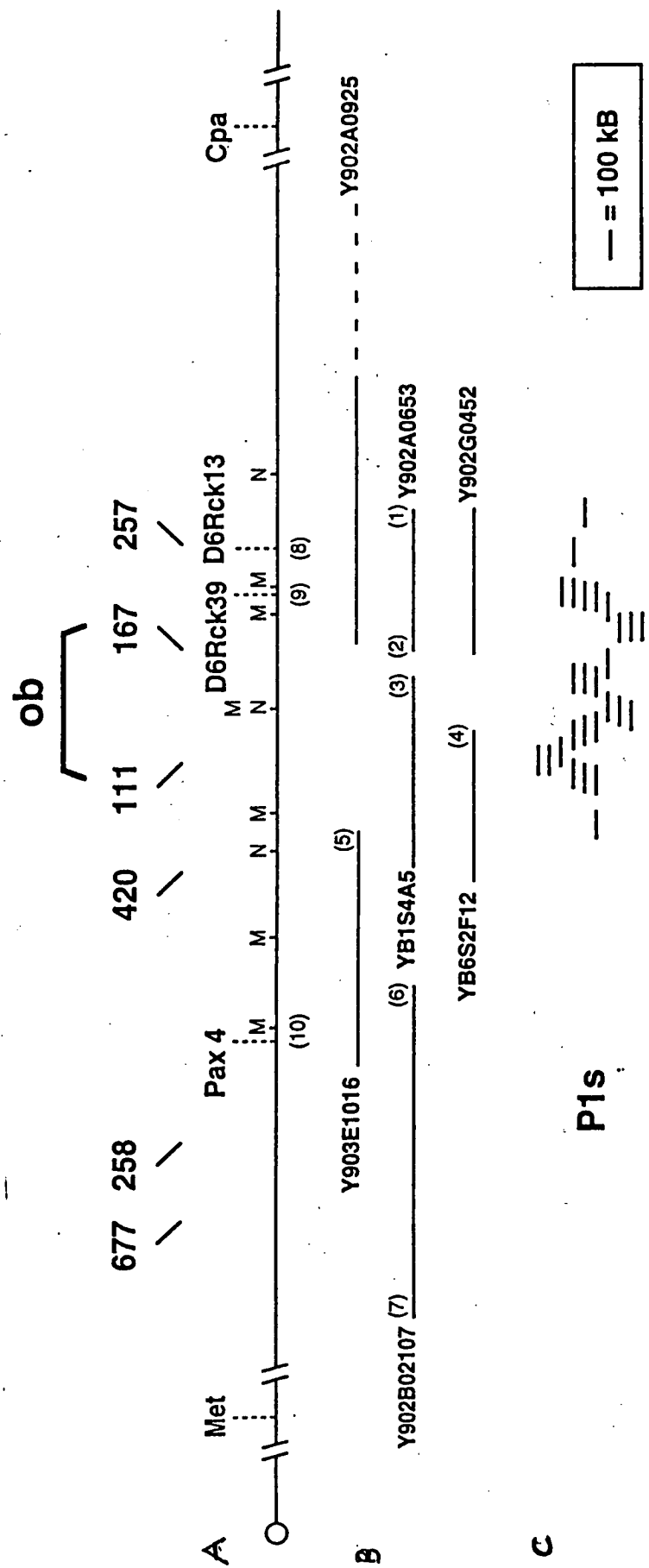


Figure 8

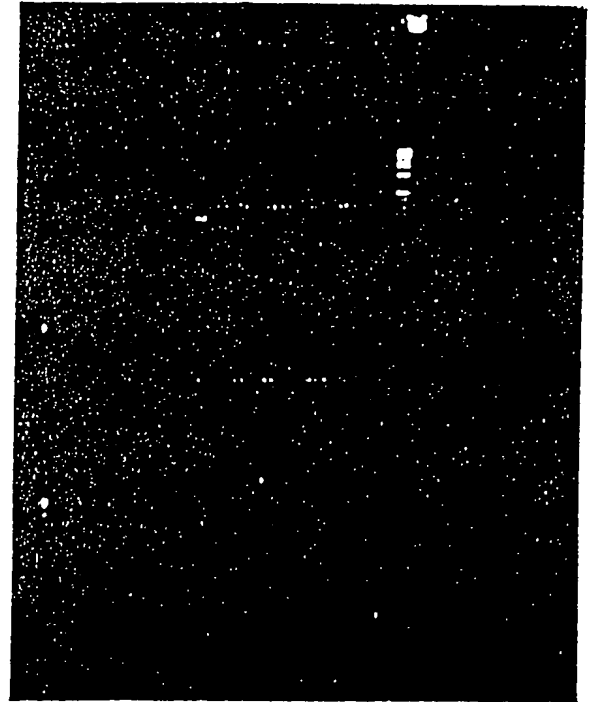
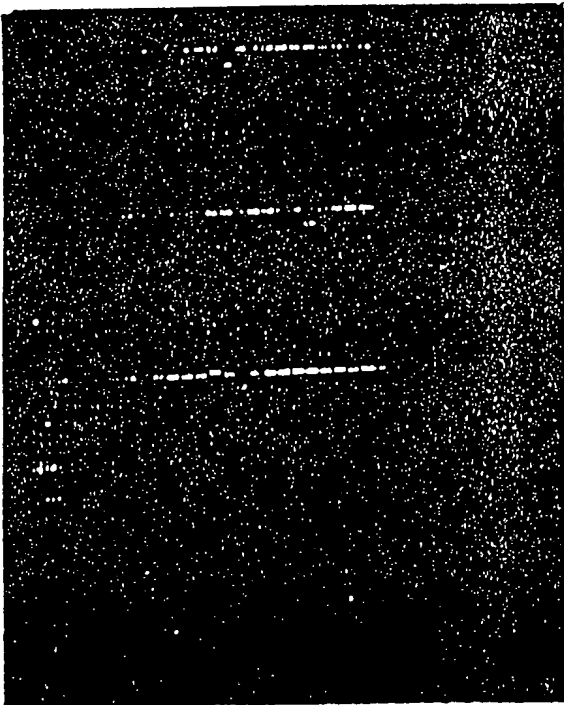




Figure 9

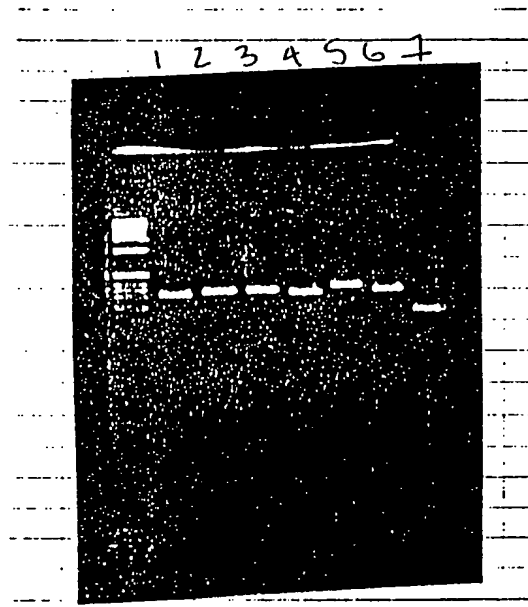


Figure 10

	+10	+20	+30	+40
1	GTGCAAGAAG	AAGAAGATCC	CAGGGCAGGA	AAATGTGCTG
	CACGTTCTTC	TTCTTCTAGG	GTCCCCTCCT	TTTACACGAC
	+10	+20	+30	+40
51	TGTCGGGTCC	NGTGGNTTTG	GTCCTATCTG	TCTTATGTNC
	ACAGCCCAGG	NCACCNAAAC	CAGGATAGAC	AGAATACANG
	+10	+20	+30	+40
101	TATCCAGAAA	GTCCAGGATG	ACACCAAAAG	CCTCATCAAG
	ATAGGTCCTT	CAGGTCCTAC	TGTGGTTTTTC	GGAGTAGTTC
	+10	+20	+30	+40
	NCAGGATCAC	TGANATTTC	CACACG	
151	NGTCCTAGTG	ACTNTAAAGT	GTGTGC	

Figure 11A

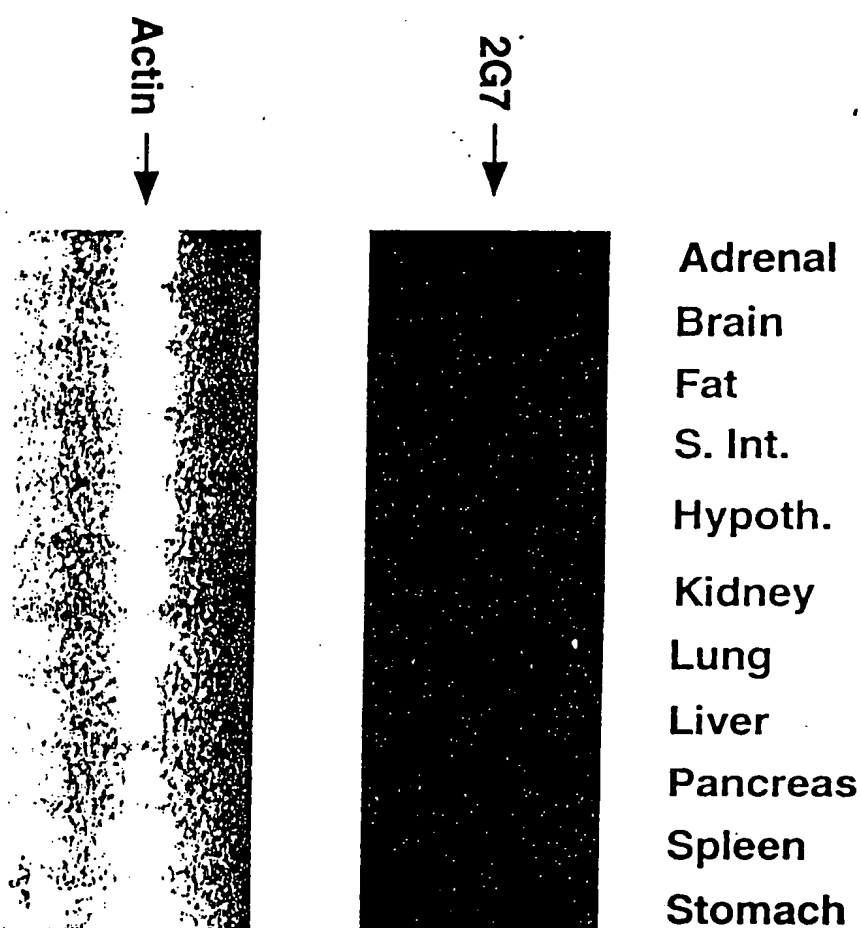


Figure 11B

185 —

285 —

white fat

brain

small intestine

stomach

pancreas

lung

testis

heart

spleen

liver

Figure 12A

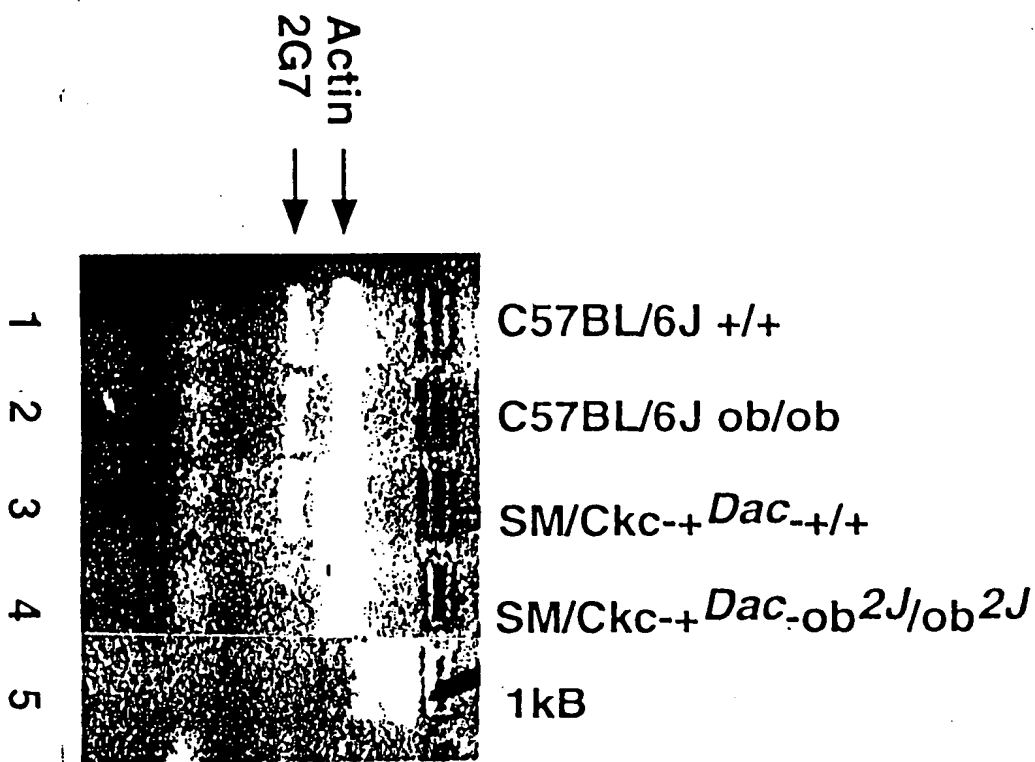


Figure 12 B

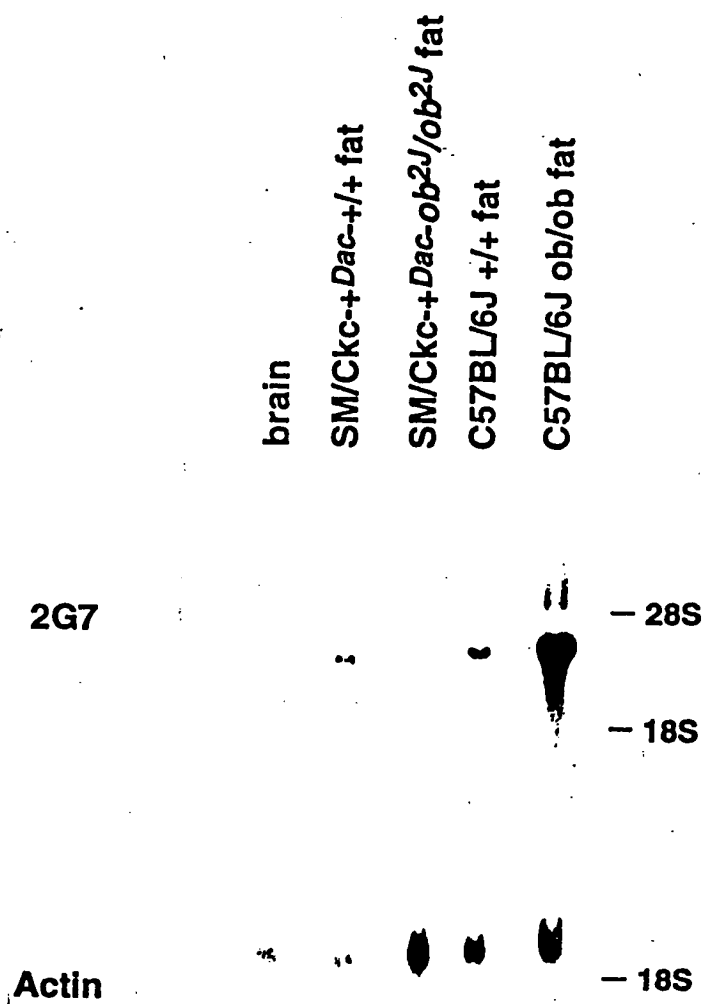


Figure 13

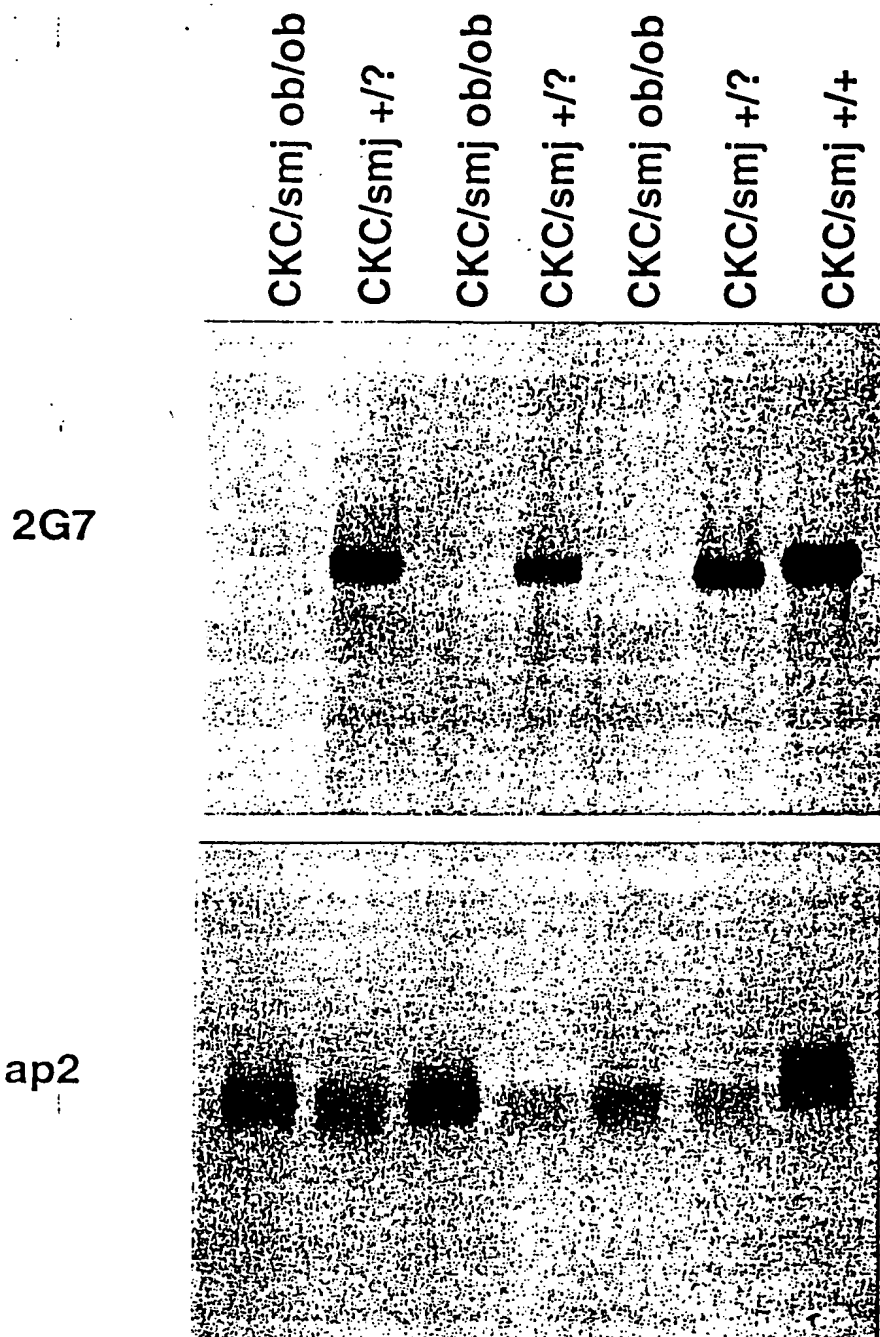


Figure 14

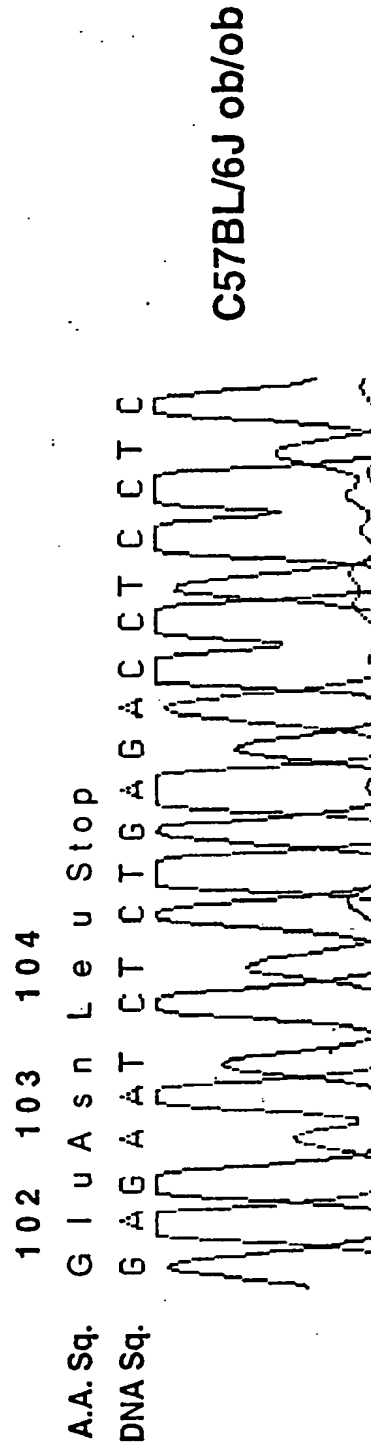
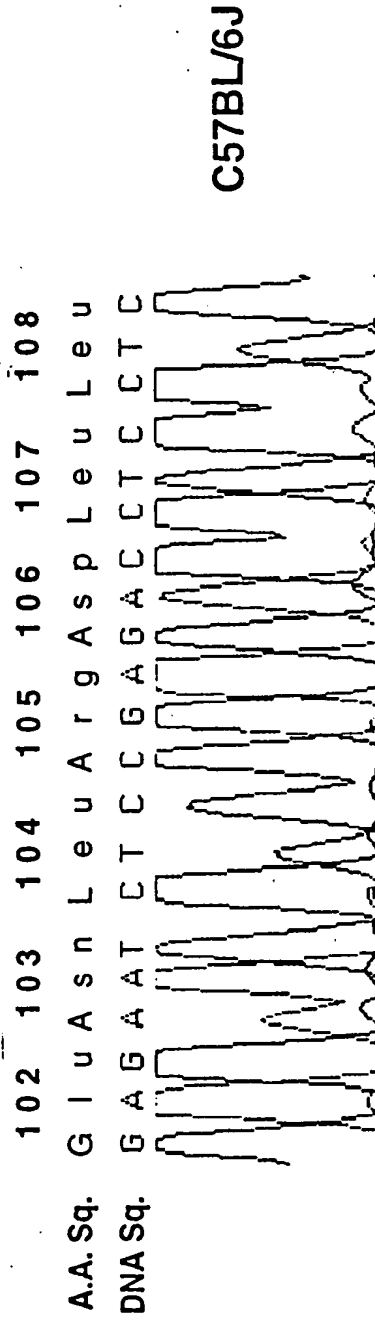




Figure 15A

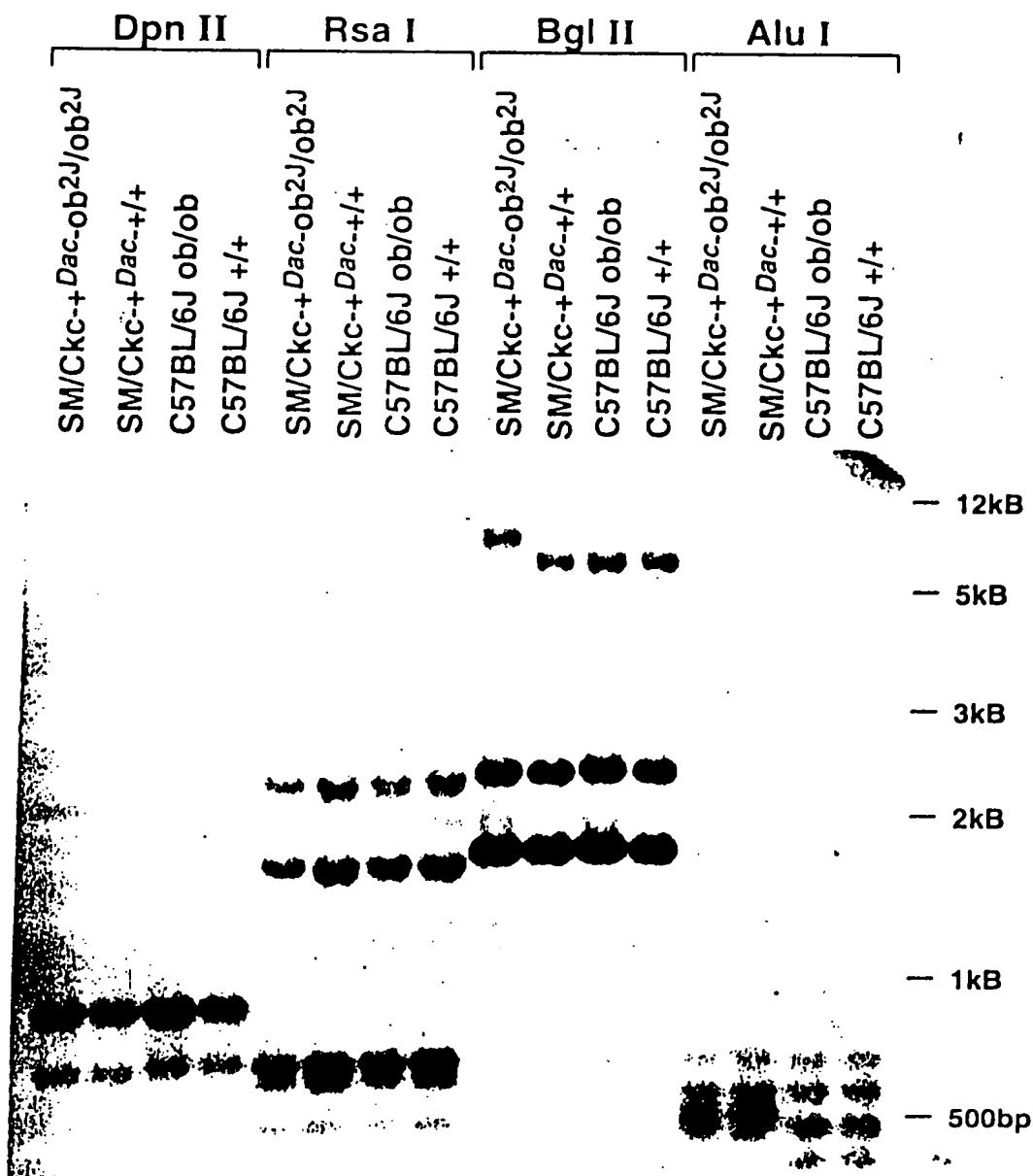




Figure 16.

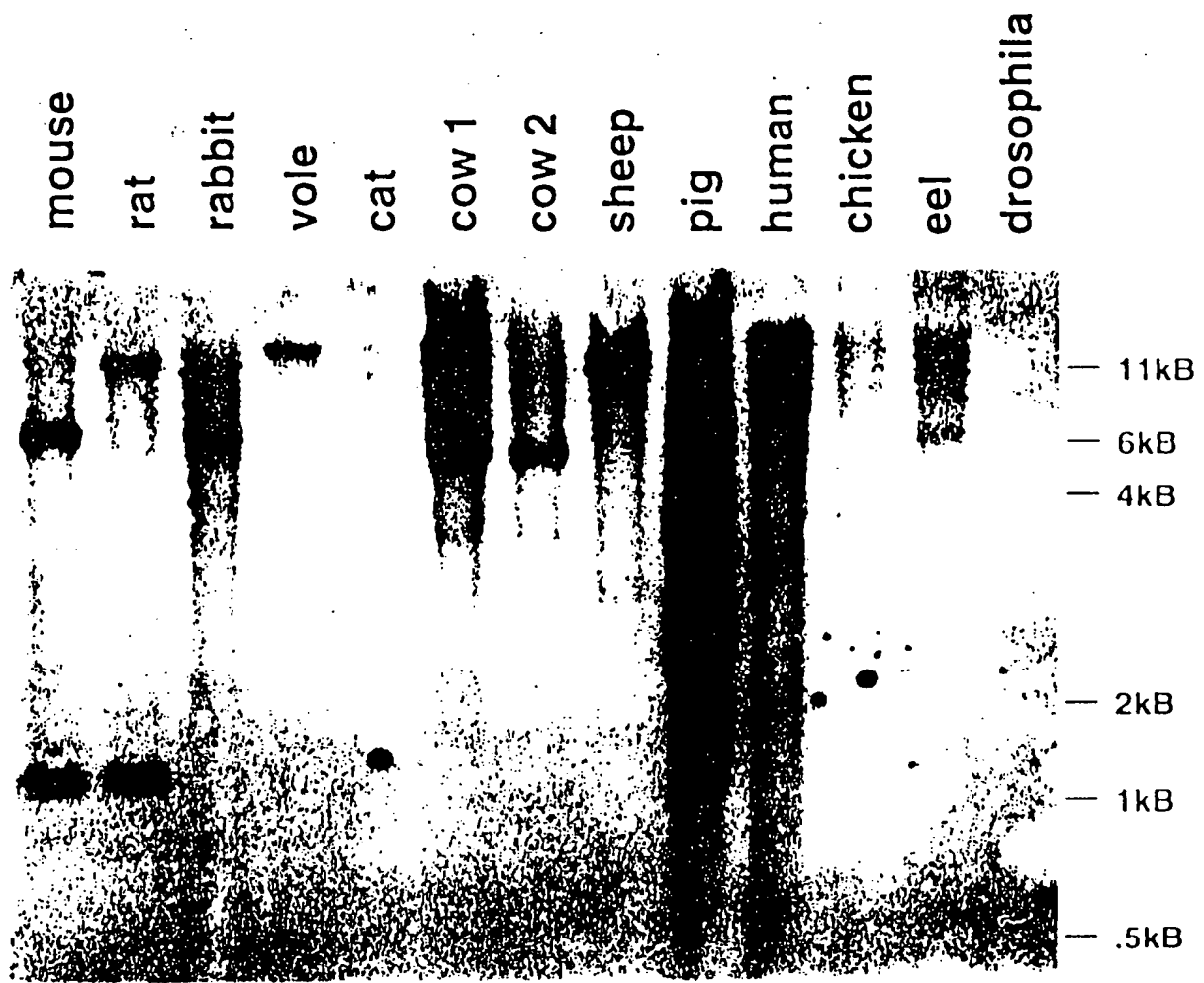


Figure 17

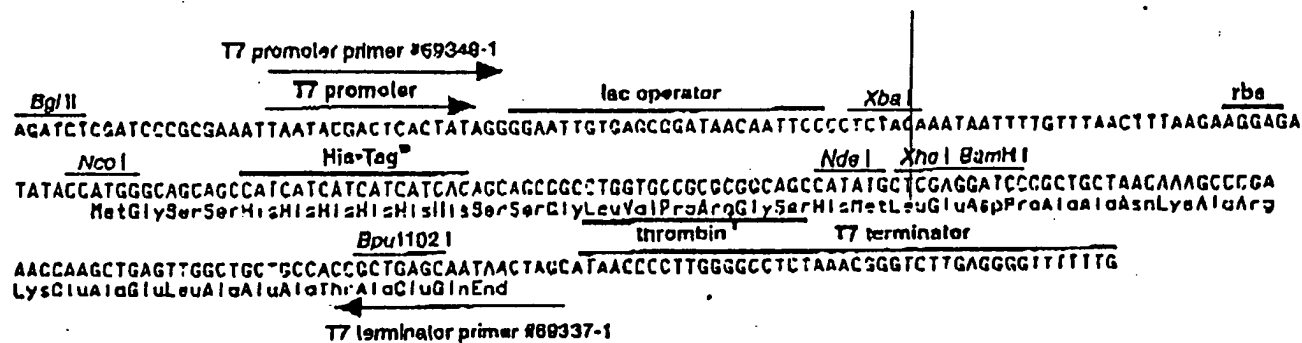
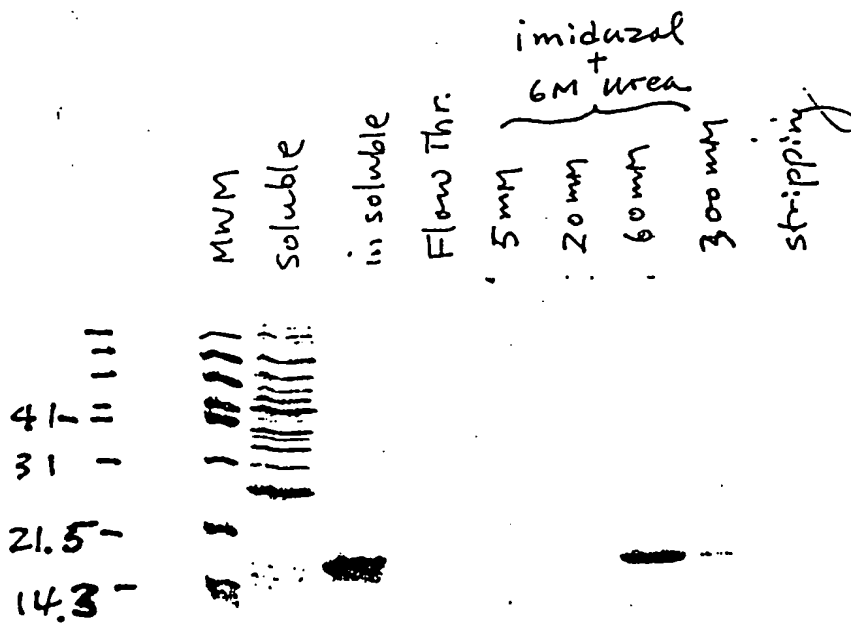


Figure 18 A



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Figure 18B

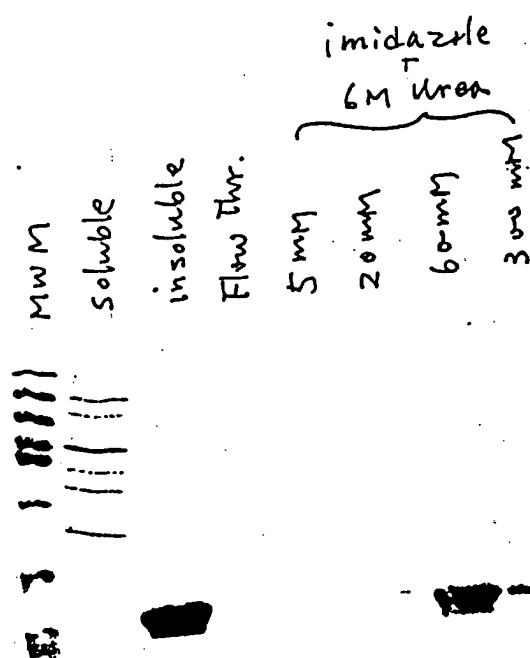
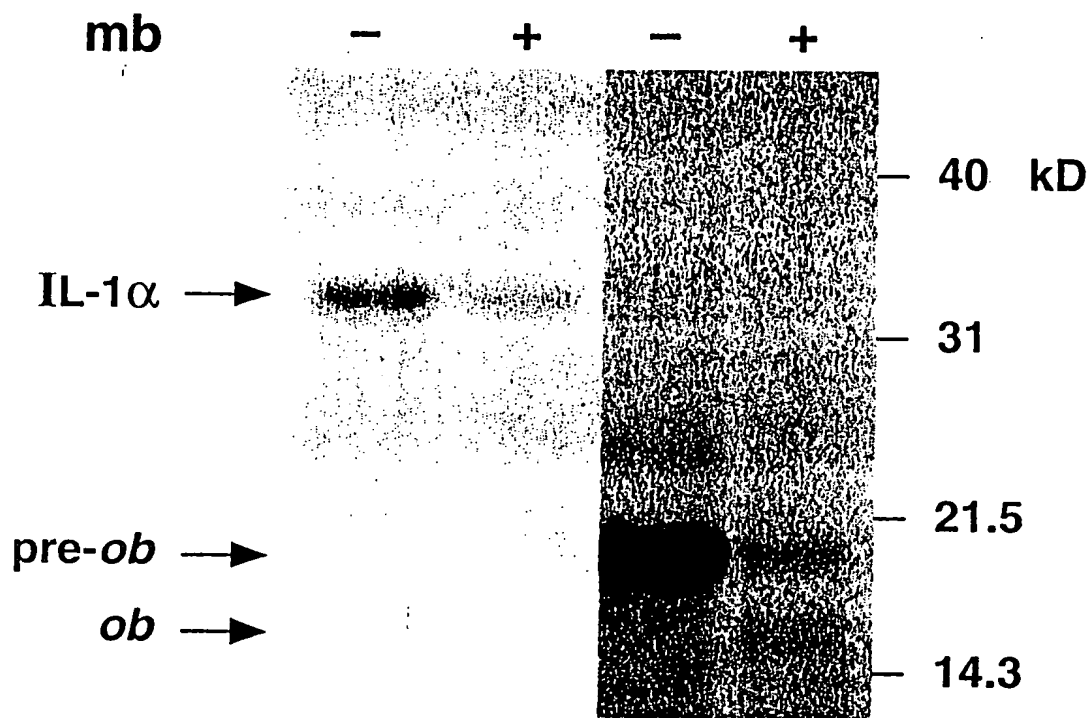


Figure 19A



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Figure 19B

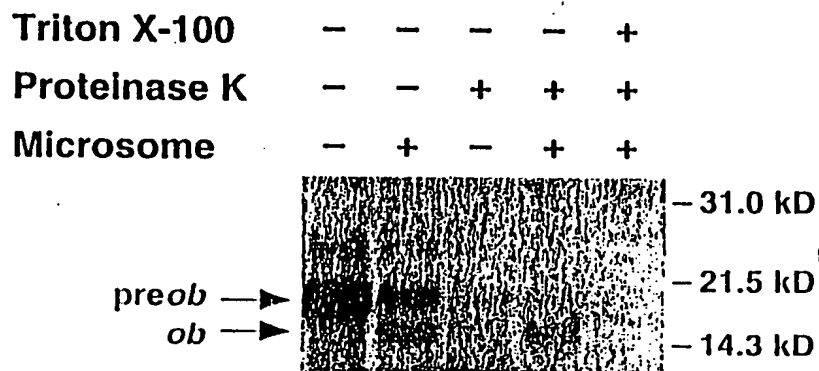




Figure 20A

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10	20	30	40	50
GGTTGCAAGG	CCCAAGAAGC	CCATCCTGGG	AAGGAAAATG	CATTGGGGAA
60	70	80	90	100
CCCTGTGCGG	ATTCTGTGG	CTTGGCCCT	ATCTTTTCTA	TGTCCAAGCT
110	120	130	140	150
GTGCCCATCC	AAAAAGTCCA	AGATGACACC	AAAACCCTCA	TCAAGACAAT
160	170	180	190	200
TGTCACCAGG	ATCAATGACA	TTTCACACAC	GTAAGGAGA	GTATGCGGGG
210	220	230	240	250
ACAAAGTAGA	ACTGCAGCCA	GCCCAGCACT	GGCTCCTAGT	GGCACTGGAC
260	270	280	290	300
CCAGATAGTC	CAAGAAACAT	TTATTGAACG	CCTCCTGAAT	GCCAGGCACC
310	320	330	340	350
TACTGCAAGC	TGAGAAGGAT	TTGGATAGC	ACAGGGCTCC	ACTCTTTCTG
360	370	380	390	400
GTTGTTTCTT	NTGGCCCCCT	CTGCCTGCTG	AGATNCCAGG	GGTTAGNGGT
410	420	430	440	450
TCTTAATTCC	TAAA	GAP OF SEQUENCE (~1.4 kb)		
460	470	480	490	500
GGTTCCTTCA	GGAAGAGGCC	ATGTAAGAGA	AAGGAATTGA	CCTAGGGAAA
510	520	530	540	550
ATTGGCCTGG	GAAGTGGAGG	GAACGGATGG	TGTGGGAAAA	GCAGGAATCT
560	570	580	590	600
CGGAGACCAG	CTTAGAGGCT	TGGCAGTCAC	CTGGGTGCAG	GANACAAGGG
610	620	630	640	650
CCTGAGCCAA	AGTGGTGAGG	GAGGGTGGAA	GGAGACAGCC	CAGAGAATGA
660	670	680	690	700
CCCTCCATGC	CCACGGGGAA	GGCAGAGGGC	TCTGAGAGCG	ATTCTTCCA
710	720	730	740	750
CATGCTGAGC	ACTGTTCTC	CCTCTTCCTC	CTNCATAGCA	GTCAGTCTCC
760	770	780	790	800
TCCAAACAGA	AAGTCACCGG	TTGGACTTC	ATTCTTGGGC	TCCACCCCAT
810	820	830	840	850
CCTGACCTTA	TCCAAGATGG	ACCAGACACT	GGCAGTCTAC	CAACAGATCC
860	870	880	890	900
TCACCAGTAT	GCCTTCAGA	AACGTGATCC	AAATATCCAA	CGACCTGGAG

910	920	930	940	950
AACCTCCGGG	ATCTTCTTCA	CGTGCTGGCC	TTCTCTAAGA	GCTGCCACTT
960	970	980	990	1000
GCCCTGGGcC	AGTGGCCTGG	AGACCTTGA	CAGCCTGGGG	GGTGTCTTGG
1010	1020	1030	1040	1050
AAGCTTCAGG	CTACTCCACA	GAGGTGGTGG	CCCTGAGCAG	GCTGCAGGGG
1060	1070	1080	1090	1100
TCTCTGCAGG	ACATGCTGTG	GCAGCTGGAC	CTCAGCCCTG	GGTGCTGAGG
1110	1120	1130	1140	1150
CCTTGAAGGT	CACTCTTCT	GCAAGGACTA	CGTTAAGGGA	AGGAACCTCTG
1160	1170	1180	1190	1200
GcTTCCAGGT	ATCTCCAGGA	TTGAAGAGCA	TGTCATGGAC	ACCCCTTATC
1210	1220	1230	1240	1250
CAGGACTCTG	TCAATTTCCT	TGACTCCTCT	AAGCCACTCT	TCCAAAGG

Figure 20B

MOUSE OB STRUCTURE

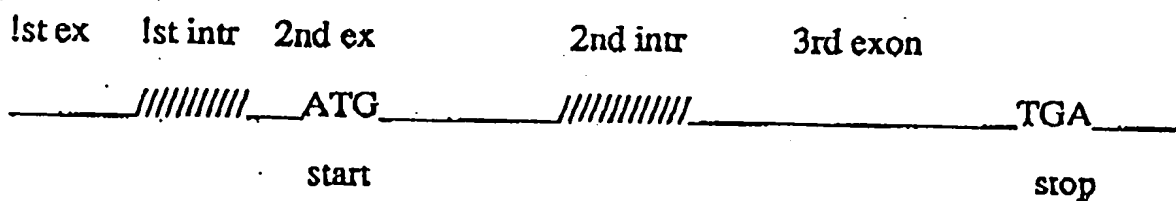


Figure 20c

HUMAN OB STUCTURE

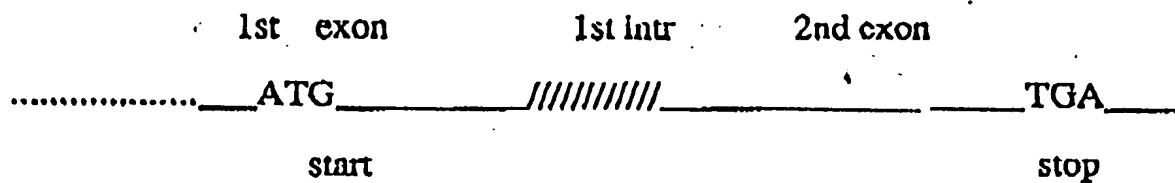


Figure 21A

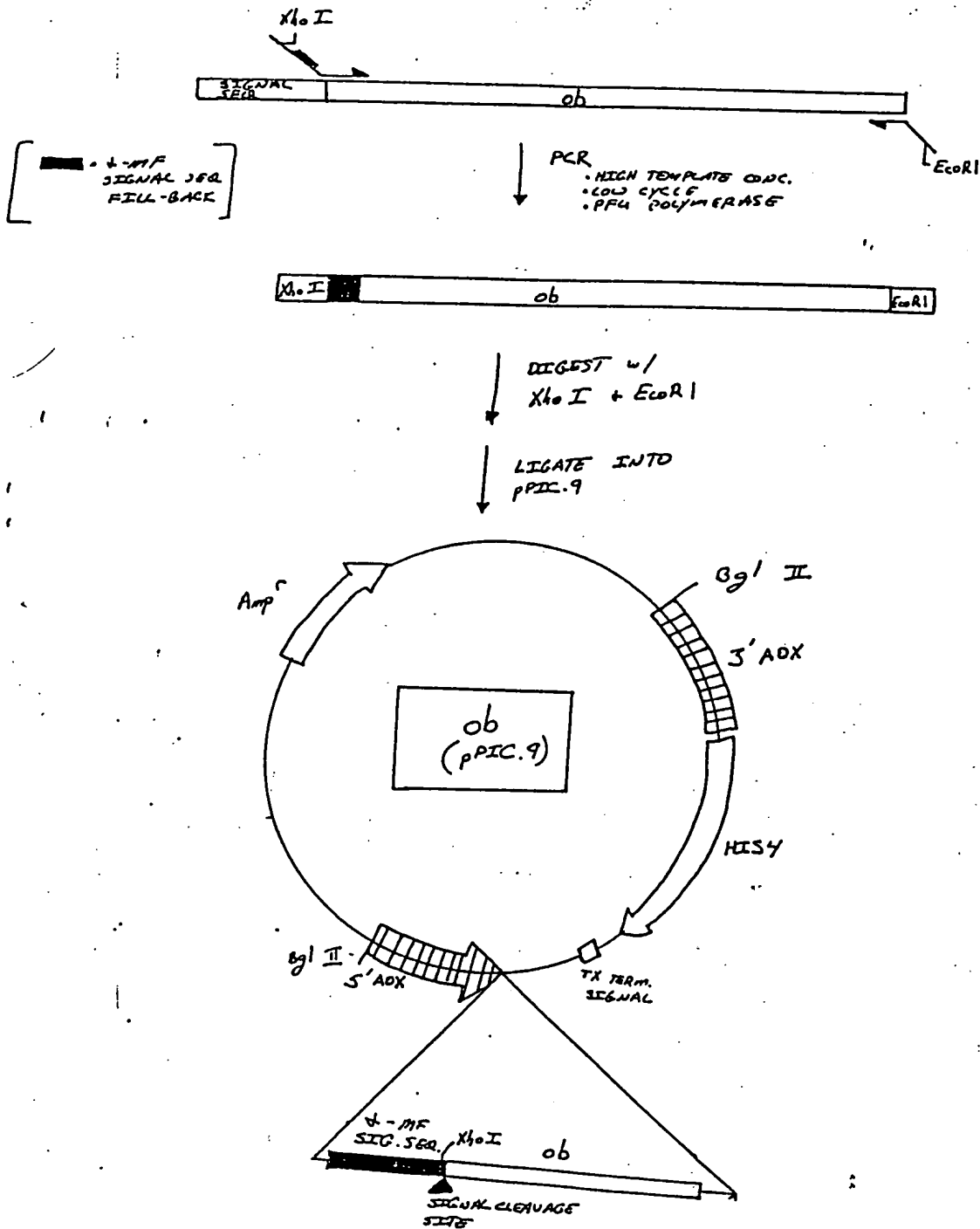


Figure 21 B

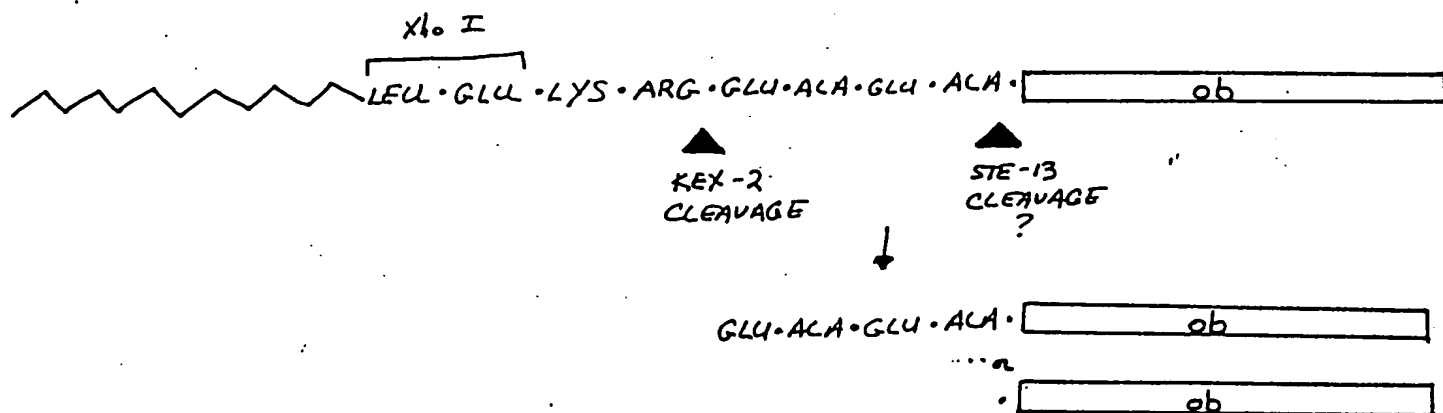


Figure 21 c

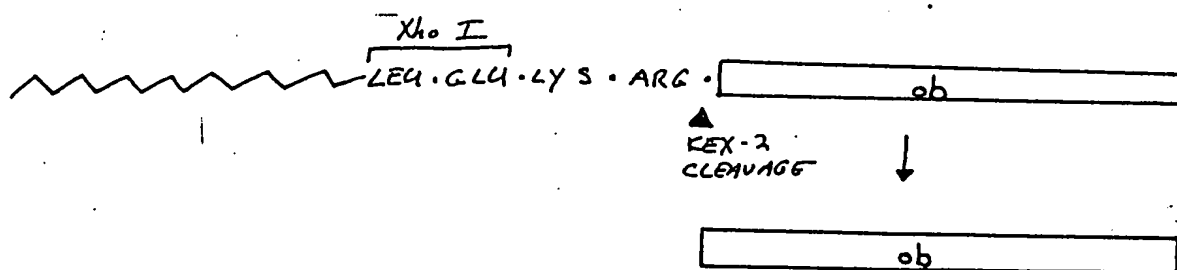


Figure 22A

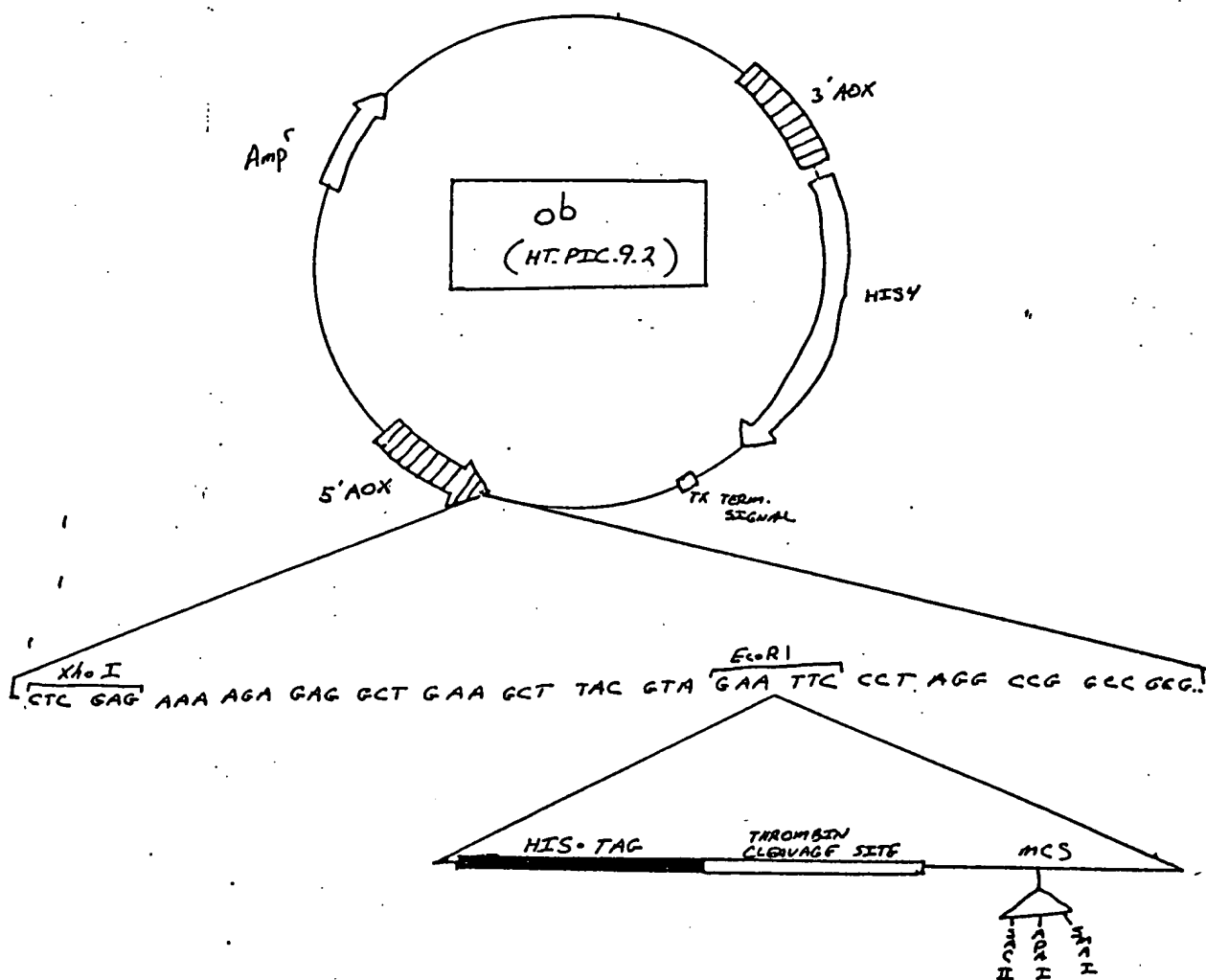


Figure 22B.

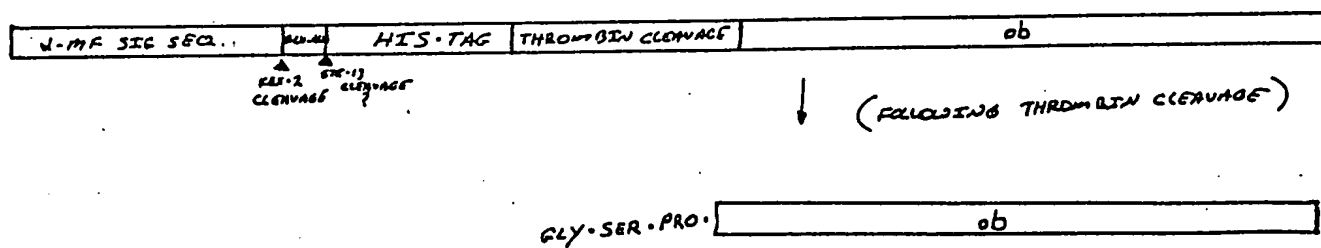


Figure 23A-

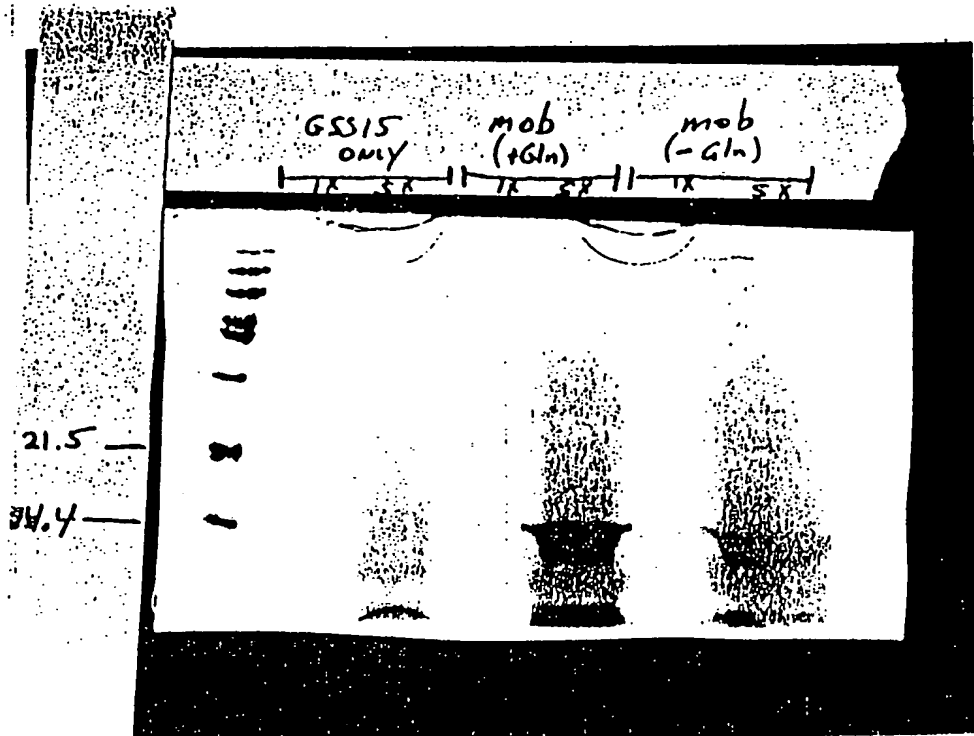


Figure 23B



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Figure 24 A

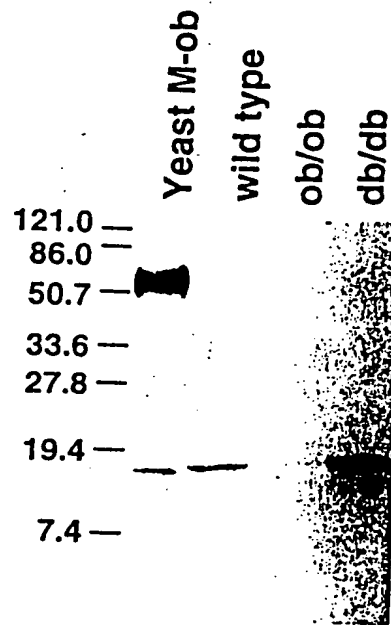
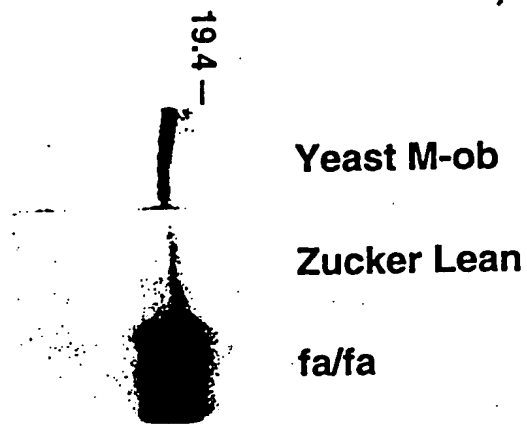
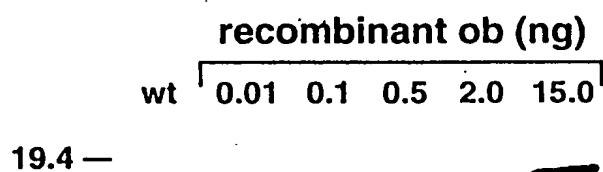




Figure 24B



## Figure 24C



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# Figure 24 D

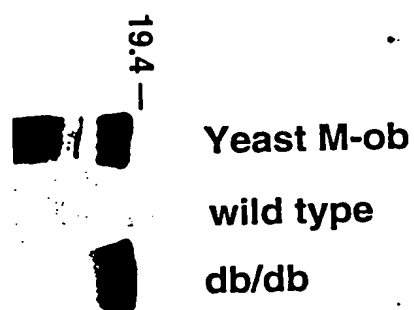


Figure 25A

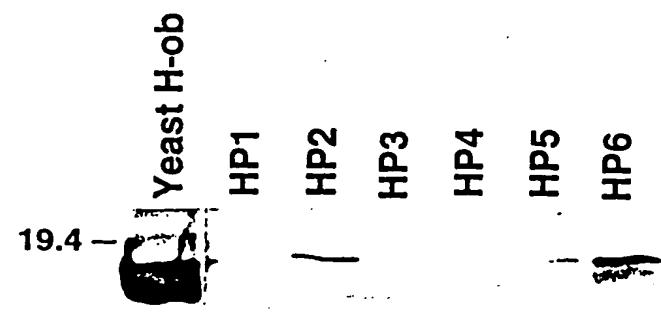


Figure 25 B

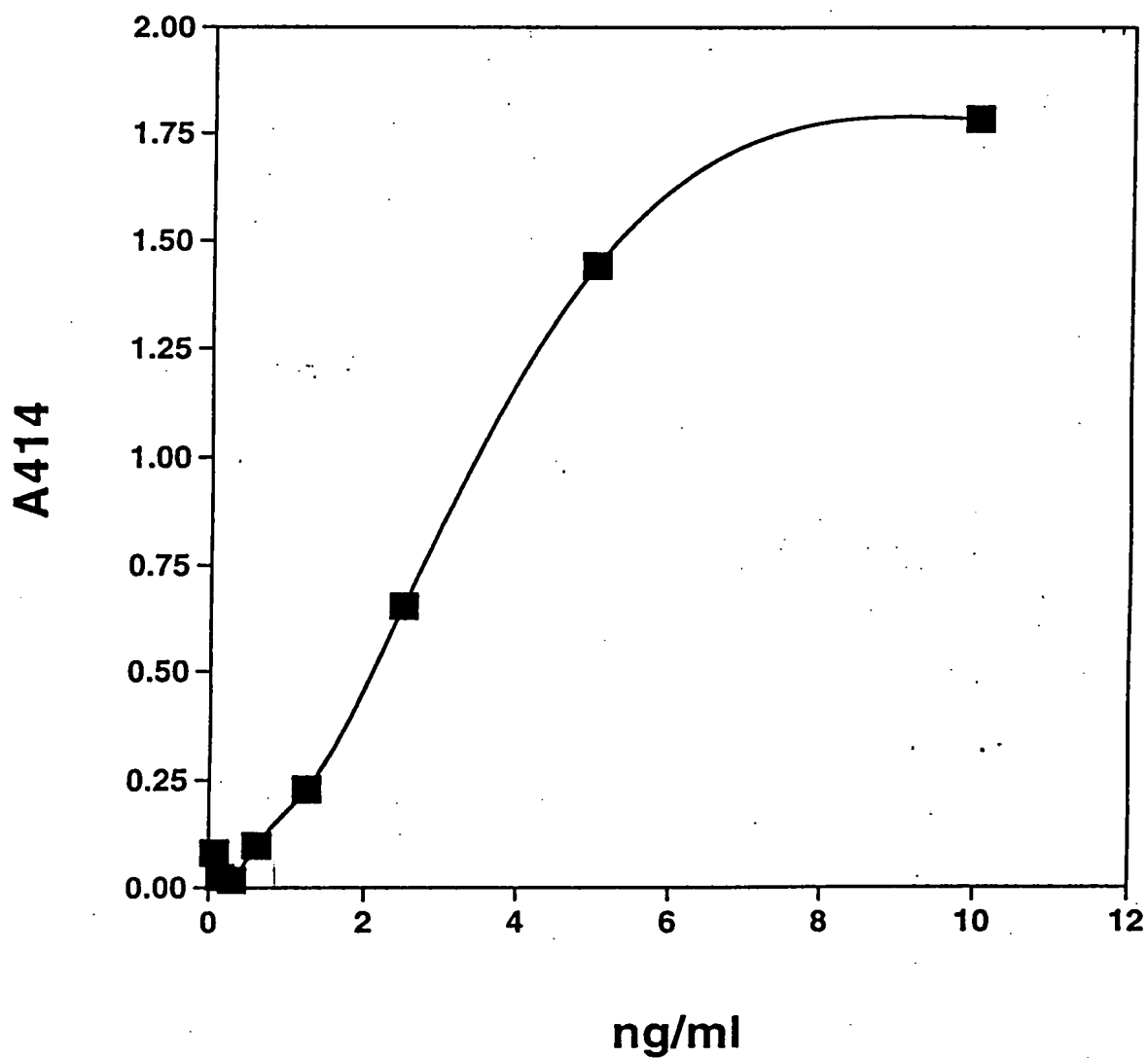
**ELISA STANDARD CURVE**

Figure 25c

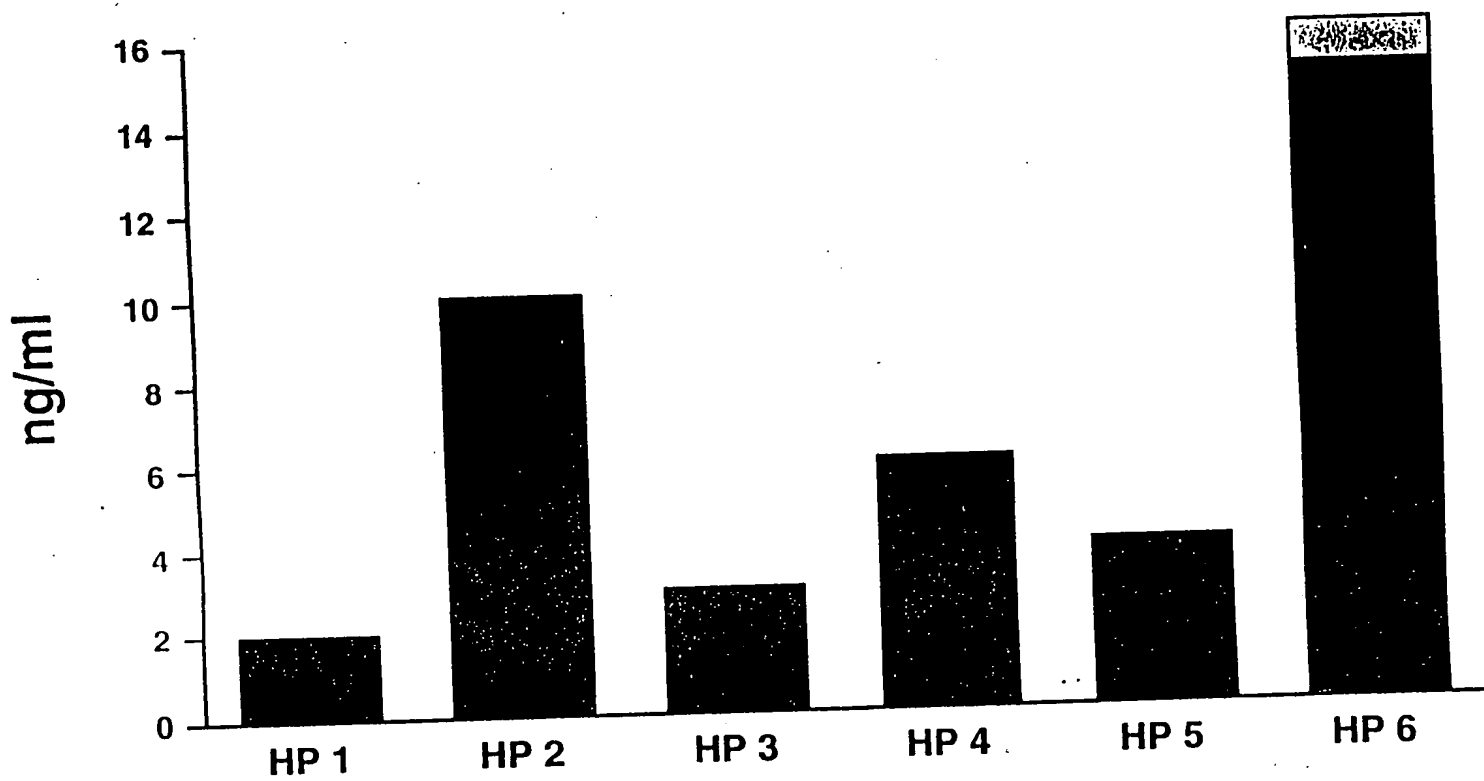


Figure 26A

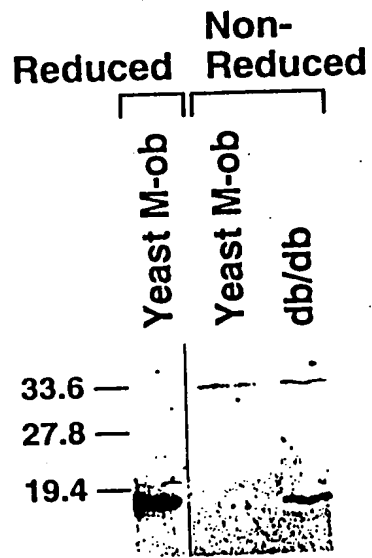
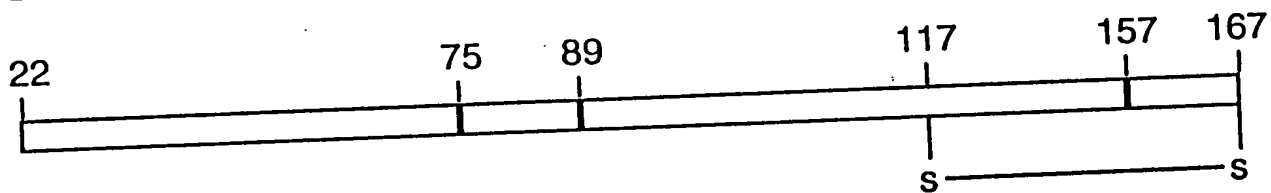


Figure 26 B

Human ob

<u>Peptide</u>	<u>Mass(Da)</u>	
	Expected	Observed
22-167	16,024	16,024 $\pm$ 3
22-75	5936.9	5936.6 $\pm$ 1
76-89	1562.7	N.D.
90-167	8434.5	8435.6 $\pm$ 1
158-167	1131.9	N.D.



Figure 27

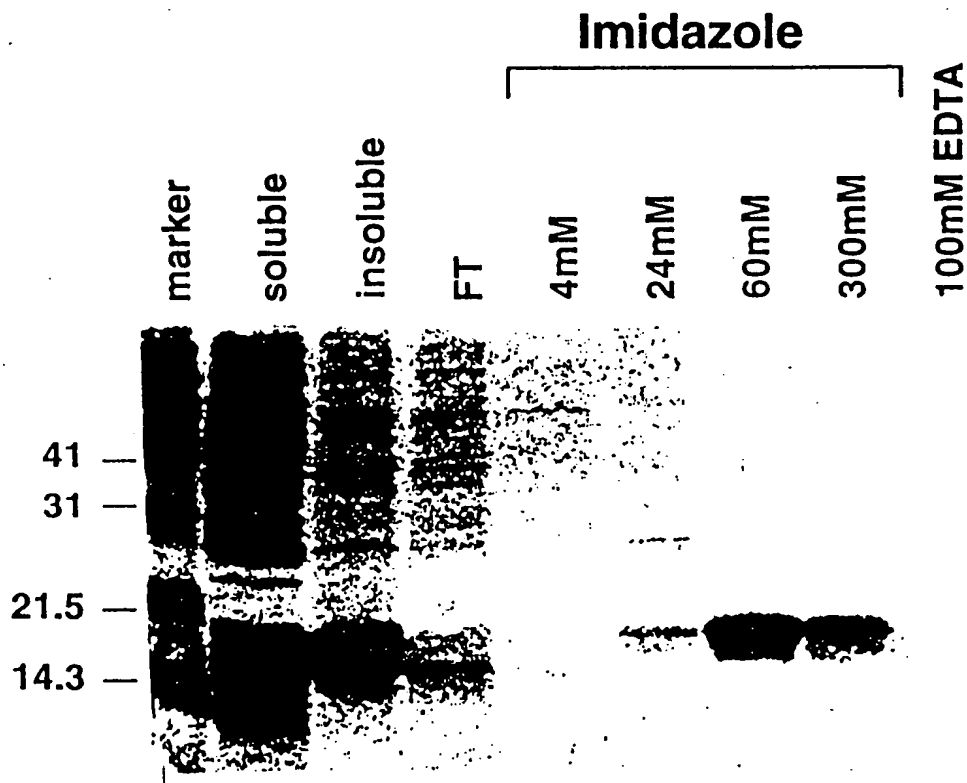


Figure 28

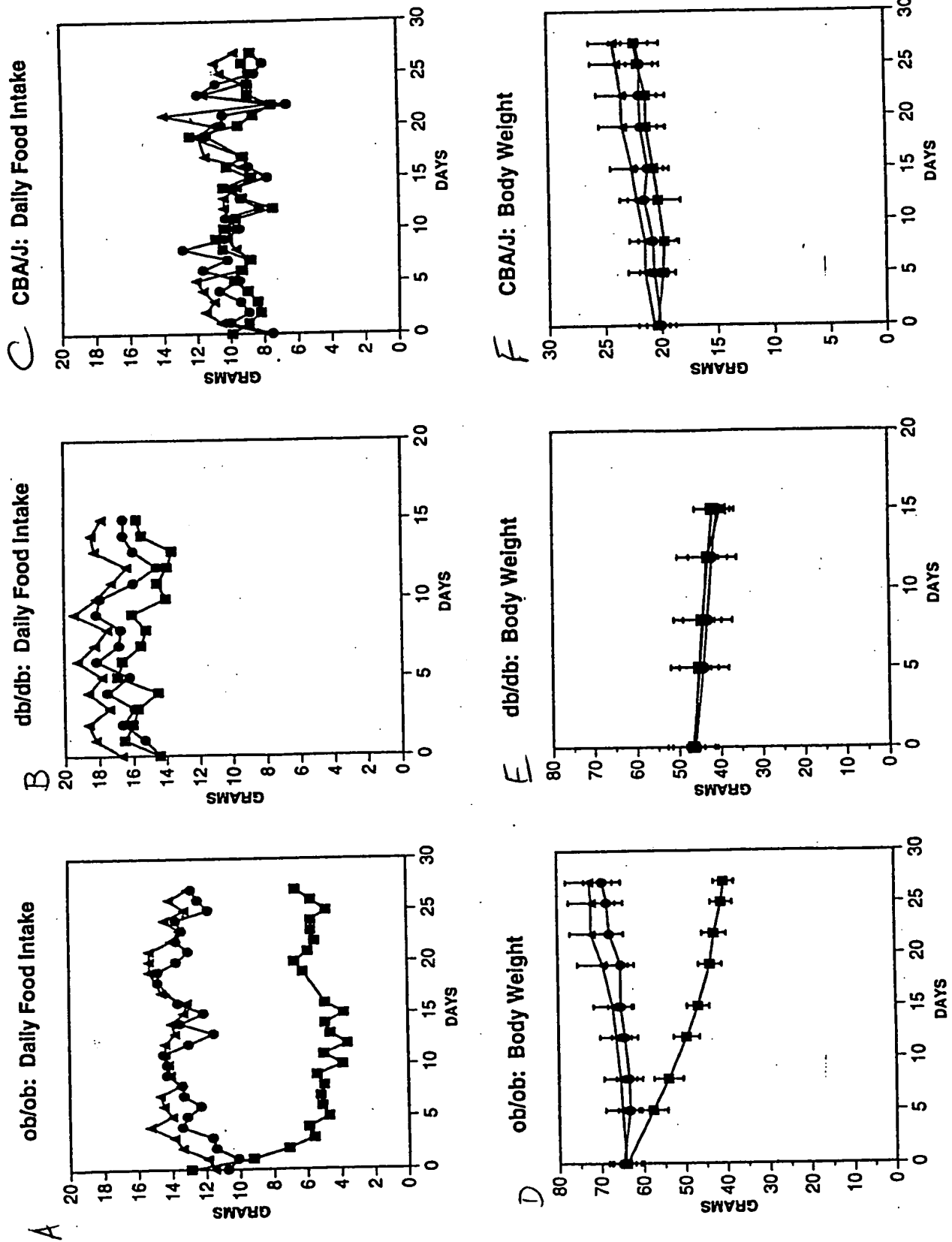


Figure 29A

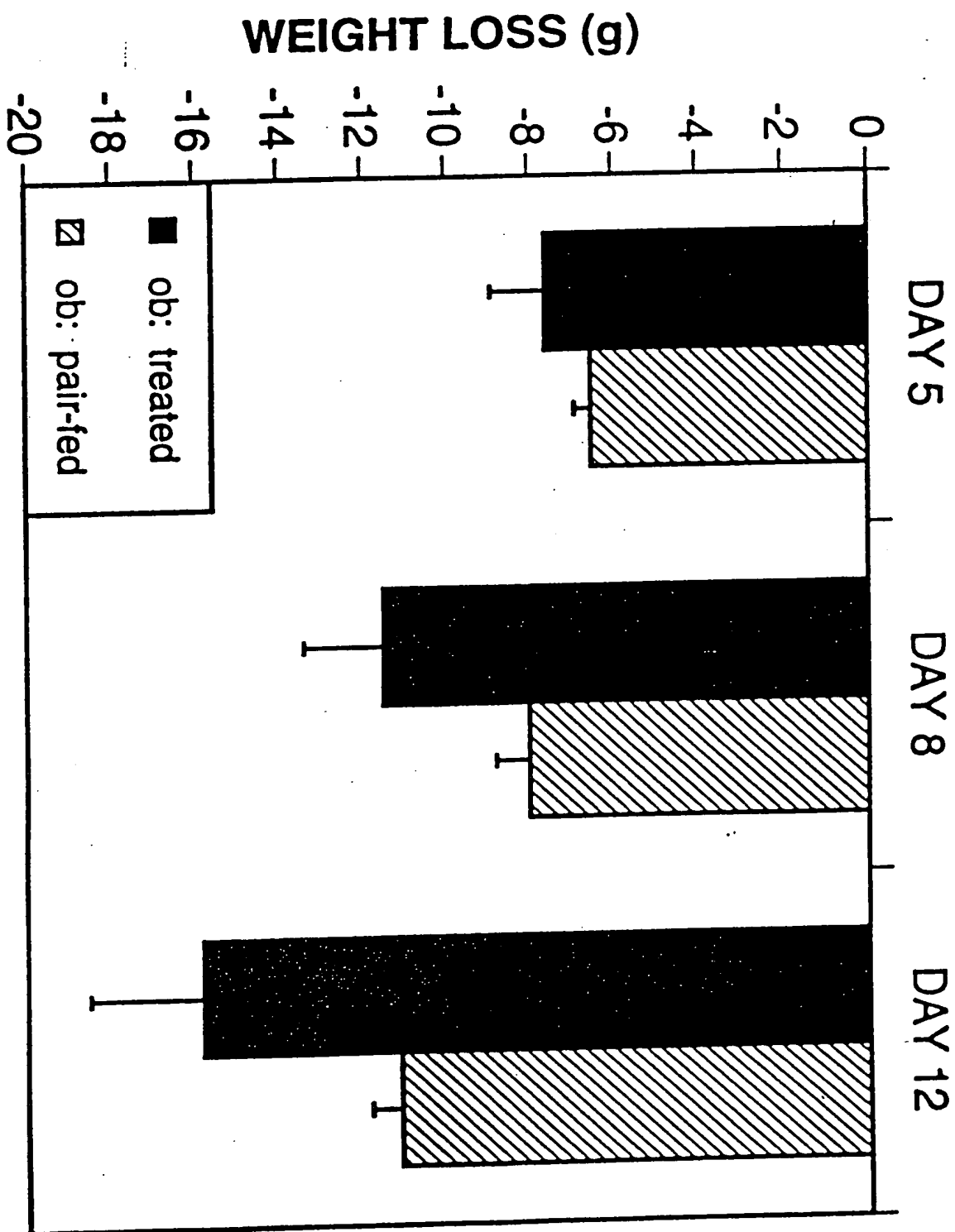


Figure 29 B



Figure 29C



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Figure 30

Wt



db/db

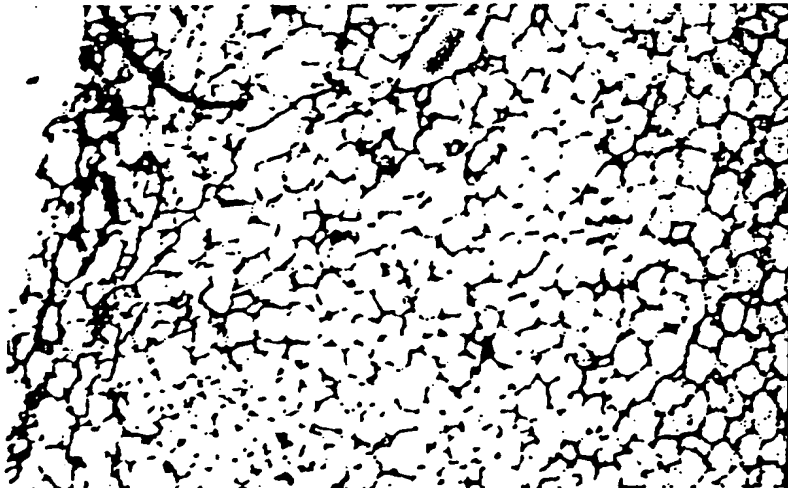


Figure 31

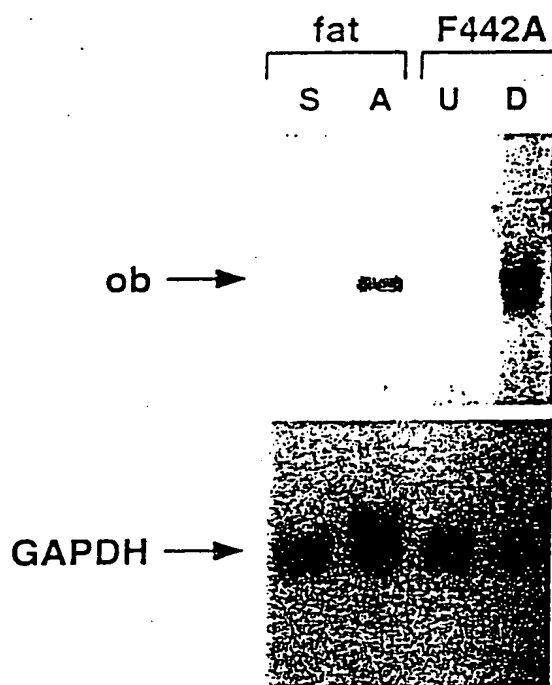


Figure 32A

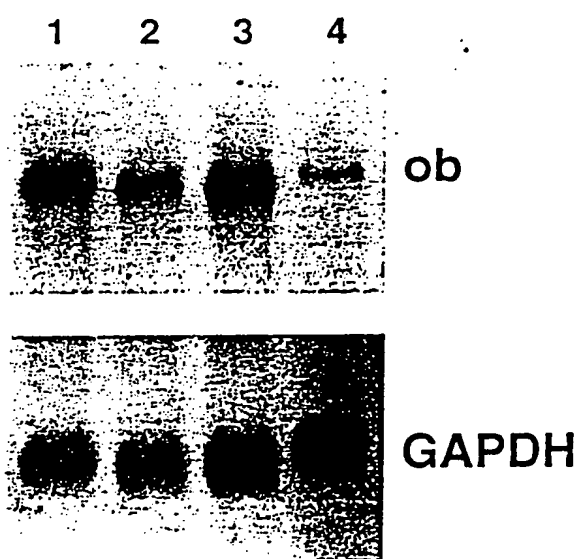




Figure 32 B



Figure 33

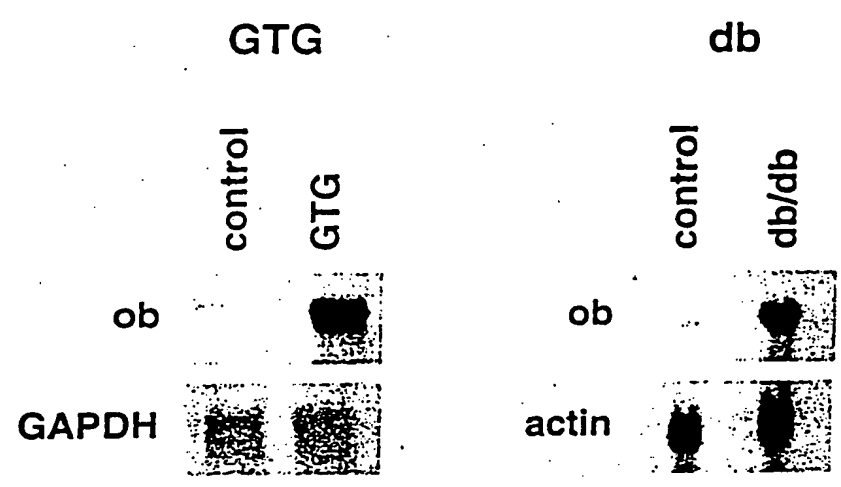
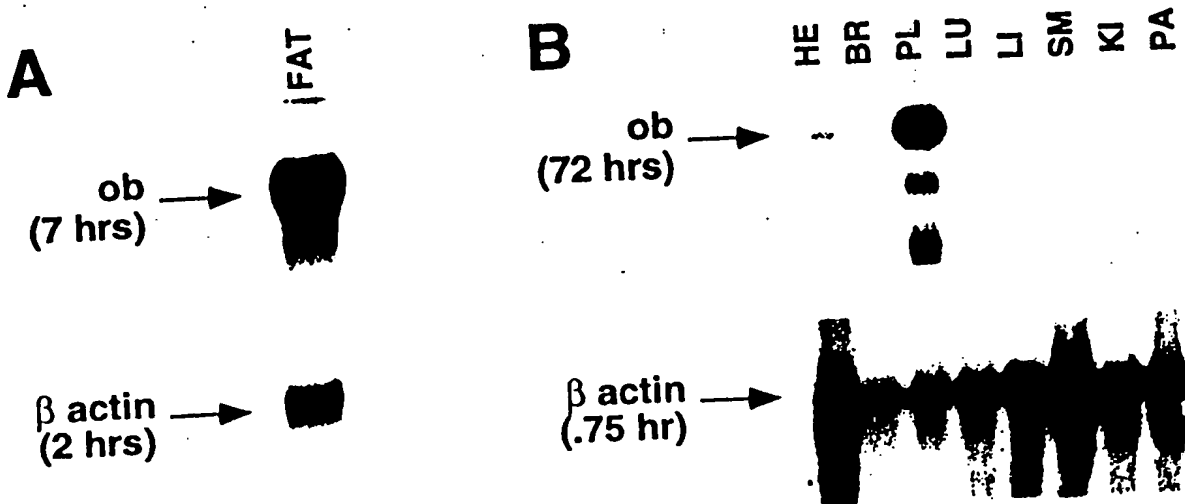
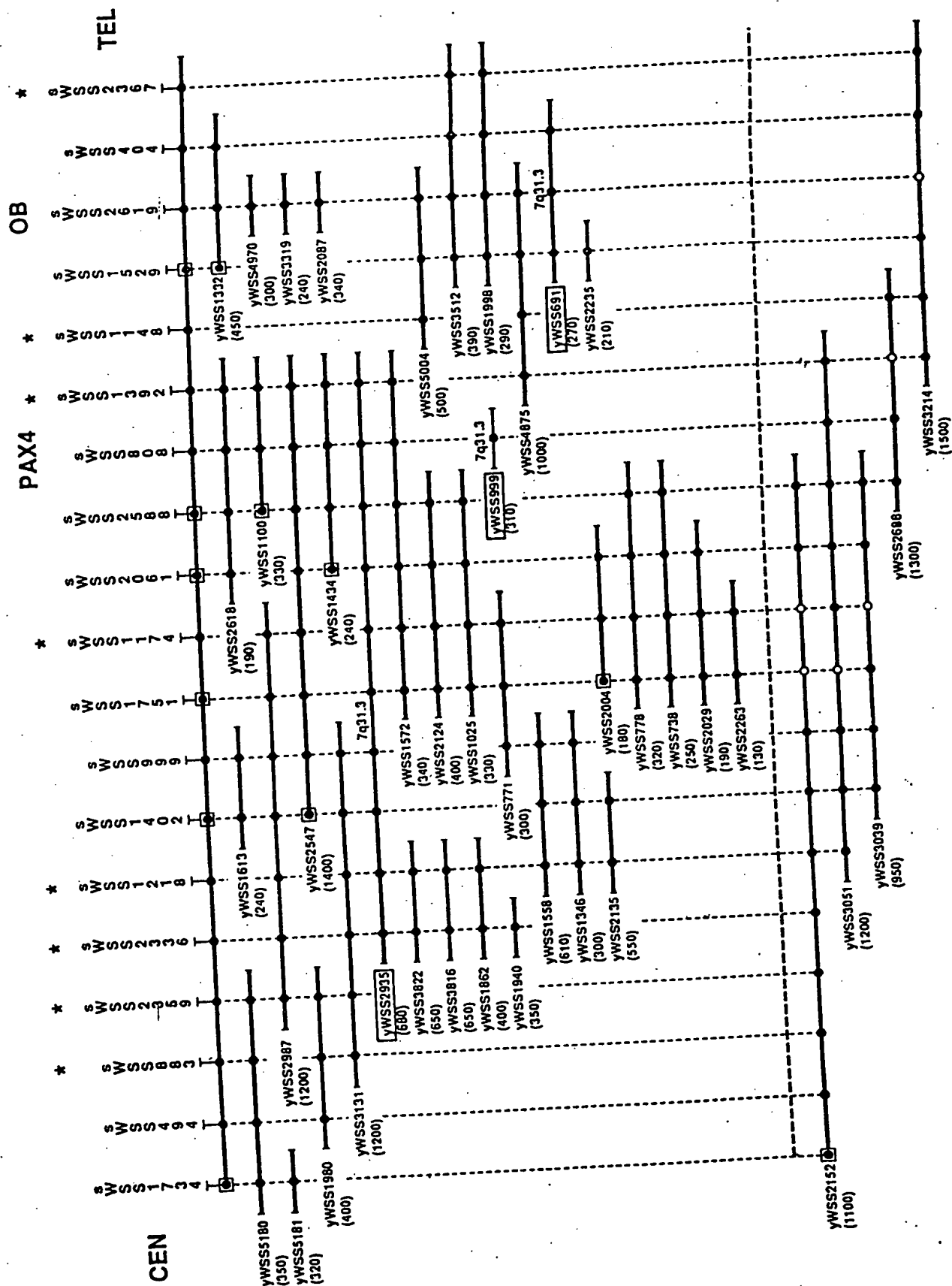


Figure 34:



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